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| 09/965,697 | 09/27/2001 | Tarlochan Singh Dhadialla | A9526 | 4412 |
| 60/394 | 7590 | 05/28/2008 | | |
| SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE WASHINGTON, DC 20037 | | | | |
| EXAMINER | | | | |
| SHAFFER, SHULAMITH H | | | | |
| ART UNIT | | PAPER NUMBER | | |
| 1647 | | | | |
| NOTIFICATION DATE | | DELIVERY MODE | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

09/965,697

Applicant(s)

DHADIALA ET AL.

Examiner

SHULAMITH H. SHAFER

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Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 February 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6-12, 14, 15 and 21-47 is/are pending in the application.
- 4a) Of the above claim(s) 21-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-12, 14, 15 and 47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 September 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 2/11/08
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notices of Informal Patent Application
- 6) ☐ Other: _____

Detailed Action

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647. The Examiner prosecuting this application has been changed. Any inquiries relating to the examination of the application should be directed to Shulamith H. Shafer, Art Unit 1647.

Status of Application, Amendments, And/Or Claims:

Applicant's response, of 11 February 2008, is acknowledged and has been entered. Claims 5, 13, 16-20 are canceled. Claims 21-47 are newly presented

Newly presented claims 21-46 are drawn to multiple gene regulation systems which recite limitations not previously presented. The claims are drawn to a system comprising three hybrid peptides wherein the first hybrid peptide comprises a first DNA binding domain and a first ligand binding domain; the second hybrid peptide comprises a second DNA binding domain and a second ligand binding domain; the third hybrid peptide comprises a transactivation domain and a third ligand binding domain. The claims, as originally presented, did not recite fusion peptides comprising what would essentially be receptor fragment molecules; the originally presented claims are drawn to polynucleotides encoding polypeptides which comprise a DNA binding domain, a ligand binding and a transactivation domain. Furthermore, the newly presented claims recite new limitations "wherein the first and third hybrid peptides dimerize to form a first dimer in the presence of the first ligand, the second and third hybrid peptides dimerize to form a second dimer in the presence of the second ligand..." which would require new search of the art. Additionally, the new claims (e.g. 37-43) recite sequences not previously presented. These claims recite inventions that are independent or distinct from the invention originally claimed and would have been restricted from originally claimed invention and subject to requirement for election of species.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 21-46 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-4, 6-12, 14, 15 and 21-47 are pending in the instant application. Claims 21-46 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1-4, 6-12, 14, 15 and 47 are under consideration.

Information Disclosure Statement:

The information disclosure statements filed 11 February 2008 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because Reference 31 on first IDS filed on that day could not be found among the submitted documents. Reference 10 on second ID filed on that day is in Japanese; no English abstract or indication of relevant portions of the reference has been provided. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Objections

Drawings and Specification:

The drawings and the "Brief description of the Drawings" in the specification are objected to because Figure 2 is a line graph; however, the Brief Description of the Drawings (page 6, last paragraph) describes "numbers on top of bars indicate fold increase over DMSO levels". Figure 2 does not depict any bars or numbers on top of

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bars. Appropriate correction is required so that Figure 2 and Brief description refer to identical subject matter.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Maintained Rejections

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-4, 6- 12 14, and 15 as failing to comply with written description requirement is maintained and applied to newly presented claim 47 for reasons of record and for reasons set forth below. The claim (s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

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one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants traverse the rejection (reply of 11 February 2008, pages 12-14). The reasons for the rejection are:

1. Applicants claim and describe multiple inducible gene regulation systems as part of their invention (page 12 of response of 11 February 2008).
2. Applicants provide detailed instructions as to how to identify non-cross-interactive receptor-ligand pairs and how to make and isolate said pairs (reply of 11 February 2008, page 13).

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

The claims are directed to a genus of an essentially unlimited scope of multiple gene regulation systems comprising two or more individually operable gene regulation systems, wherein each individually system operates independently of any other ("is orthogonal"). However, the only systems described are ones comprising two independent systems (Examples 1 and 2), a Lepidopteran/Dipteran and a Lepidopteran/Homopteran ecdysone receptor system. Applicant has not identified any particular chemical structure that will provide the required specificity and uniqueness of binding between the ligand and the receptor for use in the claimed multiple orthogonal systems, but has identified the claimed systems solely by a function.

Applicants assert that "additional ligands and receptors for use in multiple systems arebased on the *rational modification of well characterized structures* which is taught in the specification (page 12, last paragraph of response of 11 February 2008 bridging page 13 first paragraph). Thus, applicants are not in possession of the additional ligands and receptors, but are describing methods of discovering, identifying and assaying for such. The disclosure, at pages 40-43 (and quoted in response on page 13) outline complex, art-recognized methods of searching for specific ligand and screening for novel cognate LBDs. The structures of ligands presented on page 40, as potential chemotypes ideal for use as ligands, comprise a natural ecdysteroid and a

known diacylhydrazine. These compounds appear to be cross-interactive across insect species, which is contrary to that required by the claimed invention. Applicants teach that "an orthogonal ligand/receptor set does not exist within these two structural families". This is certainly not evidence of possession but indicates that to achieve the goal of a multiple, orthogonal gene regulation system, further experimentation is required (page 40, lines 8-15).

Thus, applicants have not disclosed any additional molecules as ligands nor have they identified any particular cognate LBDs. The methods outlined act as an invitation to design and discover which ligands-receptor pairs may work as the multiple gene regulatory systems of the instant invention.

To summarize: Applicants' teachings are an invitation to experiment to design, identify and isolate appropriate receptor/ligand pairs which act orthogonally; the disclosure does not provide evidence that Applicants were in possession of such.

The situation is analogous to that decided in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), which states

"an adequate written description of a DNA [product] requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself".

Accordingly, the court held in *Univ. California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed Cir 1997) that:

"One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or identify the members of the genus. A definitions by function....does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is"

An invitation for others to discover a representative number of species with known or disclosed correlation between function and structure of the polynucleotides or polypeptides of gene modulation systems or by a combination of such identifying characteristics does not reasonably provide one of skill in the art with sufficient information to reasonably visualize or predict which ligand/receptor pairs would be encompassed by the claims. Therefore, Applicants are not in possession of the claimed

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genus of "multiple inducible gene modulation system" and thus, the current claims do not comply with the requirement for written description under 35 USC 112, first paragraph.

As stated in previous Office Action, only the Lepidopteran/Dipteran and Lepidopteran/Homopteran ecdysone receptor scheme, but not the full breadth of the claims meet the written description provision of 35 USC 112, first paragraph.

Conclusions:

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHULAMITH H. SHAFER whose telephone number is (571)272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao, Ph.D. can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shulamith H. Shafer, Ph.D./

Examiner, Art Unit 1647

/Lorraine Spector/ Ph.D.

Primary Examiner, Art Unit 1647